REMARKS

Upon the entry of this Amendment, Claims 1-4, 6-10, 13, 23-24, and 26-28 are all the claims pending in this application. Claims 5, 11-12, 14-22 and 25 are canceled. Claims 1-4, 8-9 and 23 have been amended, and new Claims 26-28 have been introduced. Support for the Claim amendments may be found throughout the specification and originally filed claims.

Specifically, Claims 1, 3-4, 8-9 and 23 have been amended i) to specify the originally claimed formula (I) to be of formula (VI) or (VII) and ii) to specify the originally claimed chemotherapeutic agent to be a platinum-based or anti-mitotic agent. Support for the amendments to Claims 1, 4, 8-9 and 23 can be found at least at page 3, pages 17-18, in Examples 1 and 2, and in original Claims 1, 4, 8-9, 13 and 23-24.

Claim 2 has been amended to clarify the language, and support for the amendment to Claim 2 can be found at least in original Claims 1-2.

New Claims 26-28 have been introduced to specify the originally claimed cancer cells and tumour, and support for new Claim 26-28 can be found at least in pages 26-27, Example 1 and original Claims 6-7.

Therefore, no new matter is added by way of this amendment. Entry and consideration of the Amendment are respectfully requested.

I. Preliminary Matters

Applicants thank the Examiner for returning signed and initialed copies of the PTO Forms SB/08 that accompanied the Information Disclosure Statements filed April 3, 2007 and April 4, 2005.

In the Office Action Summary, however, it appears that the Examiner inadvertently did not acknowledge the claim for foreign priority and receipt of the certified copy of the priority document filed on April 4, 2005. Applicants request that the Examiner acknowledge Applicants' claim to priority and receipt of the certified copy of the priority document in the next action.

II. Claims 1-4 and 6-13 are Adequately Described Under 35 U.S.C. § 112

Claims 1-4 and 6-13 are rejected under 35 U.S.C. § 112, first paragraph, for lack of enablement. Specifically, the Examiner asserts that the specification, while being enabling for treating ovarian cancer with dehydroequol and cisplatin, allegedly does not reasonably provide enablement for increasing the sensitivity of cancer cells or tumors to a chemotherapeutic agent in general.

In making the rejection, the Examiner states, "[t]he claims are broad in so far as they are related to increasing the sensitivity of cancer cells or a tumor, generally, to chemotherapeutic agents, generally, using a broad range of isoflavonoid compounds."

In response, Applicants have amended the independent claims to specify that i) the chemotherapeutic agents are a platinum-based agent or an anti-mitotic agent and ii) the isoflavonoid compounds are those having formula (VI) or (VII). Thus, the claims as amended recite specific classes of chemotherapeutic agents and isoflavonoid compounds.

Further, the Examiner states, "[n]o reasonably specific guidance is provided concerning useful therapeutic protocols for increasing the sensitivity of cancer cells or a tumor to a chemotherapeutic agent using isoflavonoids of formula (I)."

In this regard, Applicants respectfully point out that Examples 1 and 2 demonstrate how the recited compounds can be used to increase the sensitivity of various cancer cell lines to recited chemotherapeutic agents. Specifically, the dehydroequol pre-treatment of chemo-

resistant cancer cells followed by a chemotherapeutic treatment results in a significant decrease in cancer cell viability. Page 38. Example 2 teaches that the pre-treatment of resistant cancer cells with dehydroequol followed by treatment with a platinum-based or anti-mitotic chemotherapeutic agent results in 30% and 50% decreases, respectively, in cancer cell viability. Page 38. Moreover, Example 1 establishes that the addition of dehydroequol decreases the required effective dose of the chemotherapeutic agent needed to treat various cancer cell lines. Pages 36-37. Therefore, the present specification provides reasonable guidance to increase the sensitivity of cancer cells or tumors to platinum-based or anti-mitotic chemotherapeutic agents using compounds of formula (VI) or (VII), as recited by the present claims.

For the reasons set forth above, Applicants respectfully submit that the amendment overcomes the rejection and request withdrawal of the above rejection.

III. Claims 1-4, 6-10, 13 and 23-24 are Patentable Under 35 U.S.C. § 103

Claims 1-4, 6-10, 13 and 23-24 are rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Kelly *et al.* (WO 98/1008503; "Kelly") in view of Ekwurlbe *et al.* (US 6,380,405; "Ekwurlbe").

Applicants respectfully traverse the rejection in view of the following remarks.

Applicants respectfully point out that a *prima facie* case of obviousness has not been established for several reasons, discussed below, and thus a finding of obviousness cannot be maintained.

First, in making the rejection, the Examiner cites *In re Kerkhoven* in asserting *prima facie* obvious for combining Kelly's dehydroequol and Ekwurlbe's cisplatin so as to provide a third composition for the same use, the treatment of ovarian cancer. Pages 6-7, *Office Action of August*

4, 2008. In *Kerhoven*, the claim at issue was a process of preparing a spray-dried detergent by mixing together two conventional spray-dried slurry detergents, and the court determined that Applicants failed to prove the superiority of the multi-slurry technique over the single-slurry technique. The Examiner in *Kerhoven* cites *In re Crockett* and explains, "the mere mixing of two compositions each taught for the same purpose, in the absence of a showing of unexpected results, is obvious." *In re Crockett*, 47 CCPA 1018, 279 F. 2d 274, 126 USPQ 186 (1960).

The present invention, however, is distinguished from *Kerhoven* because Applicants have proven the unexpected synergistic interaction between dehydroequol and cisplatin. Page 35, lines 8-10, and Examples 1 and 2. Applicants have measured the IC_{50} (an amount of cisplatin needed to kill a set number of cancer cells) of cisplatin and dehydroequol against various cancer cell lines. Pages 36-37. For example, the results show that, while the IC_{50} of cisplatin against the HPAC cell line is 34.5 μM and that of dehydroequol is 50.0 μM, the combination of cisplatin with only 2 μM of dehydroequol reduces the IC_{50} of cisplatin to 7.7 μM. Page 37. Moreover, when dehydroequol and cisplatin were administered *in vivo*, the combination inhibited tumor proliferation markedly more than single agent controls. Page 38, and Figures 6 and 7.

"Evidence that a compound is unexpectedly superior in one of a spectrum of common properties ... can be enough to rebut a *prima facie* case of obviousness." *In re Chupp*, 816 F.2d 643, 646, 2 USPQ2d 1437, 1439 (Fed. Cir. 1987). Therefore, Applicants assert that the claimed invention is not obvious over Kelly and Ekwurlbe because Applicants have shown unexpectedly superior results due to the synergistic interaction between dehydroequol and cisplatin.

Second, the combination of Kelly and Ekwurlbe does not teach or suggest all of the claim limitations in that neither reference recognizes that the sensitivity of cancer cells or a tumour to a chemotherapeutic agent can be increased by treatment with a recited compound. Specifically, the

combination of cited references fails to teach or suggest i) "increasing the sensitivity of cancer cells or a tumour to a chemotherapeutic agent" as recited in Claims 1-3, ii), "administering to a subject a therapeutically effective amount of a compound of formula (VI) or (VII) ... and a chemotherapeutic agent" as recited by Claims 4, 6-10 and 13, or iii) "a composition comprising a compound of formula (VI) or (VII) ... and a chemotherapeutic agent" as recited in Claims 23 and 24.

Regarding Claims 4, 6, 13, and 23-24, Applicants assert that the composition comprising the formula and the chemotherapeutic agent is a single element because the present invention cannot have a compound of formula (VI) or (VII) without a chemotherapeutic agent or a chemotherapeutic agent without the recited compound. Thus, Applicants respectfully request that the Office review each of the above elements, ii) and iii) as a single claim element. If assumed in its proper context, it will be apparent that the references, alone or in combination, fail to teach this single element for the following reasons.

Kelly teaches or suggests neither increasing cell sensitivity to chemotherapeutic agents nor a composition comprising a compound of formula (VI) or (VII) and a chemotherapeutic agent because Kelly does not disclose any chemotherapeutic agent.

Ekwurlbe does not teach or suggest increasing the cell sensitivity because Ekwurlbe is silent regarding any change of sensitivity to chemotherapeutic agents. Additionally, Ekwurlbe does not teach or suggest a composition comprising a compound of formula (VI) or (VII) and a chemotherapeutic agent because Ekwurlbe does not disclose a compound of formula (VI) or (VII).

To establish a *prima facie* case of obviousness, the combination of cited references, alone or in combination, must teach every limitation of the currently claimed invention, *In re Royka*

490 F.2d 981, 985 (C.C.P.A. 1974). For the reasons presented above, Applicants submit that neither Kelly nor Ekwurlbe, alone or in combination, teaches or suggests all the claim limitations of the invention, either explicitly or inherently. Thus, these references do not support a *prima facie* case of obviousness. Further, because the cited references do not teach all of the claim limitations, there can be no reasonable expectation of success in combining the cited references to arrive at the claimed invention. Accordingly, the combination of cited references fails to render obvious the claimed invention.

For the foregoing reasons, Applicants respectfully submit that the claims are not rendered obvious by the cited references.

Withdrawal of the rejection is respectfully requested.

IV. Obviousness-Type Double Patenting

1. Claims 1-4, 6-13, and 23-25 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-21 of U.S. Patent No. 6,649,648 in view of Ekwurlbe.

Applicants respectfully traverse for the following reasons.

Applicants note that the above U.S. Patent No. 6,649,648 is a national stage application of PCT application WO 98/1008503 to Kelly *et al.*; "Kelly"), and that the disclosure of U.S. Patent No. 6,649,648 is identical to that of Kelly.

For the same reasons set forth above with respect to WO 98/1008503, Applicants assert that U.S. Patent No. 6,649,648 in view of Ekwurlbe does not render obvious present Claims 1-4, 6-10, 13 and 23-24. Namely, the combination of U.S. Patent No. 6,649,648 and Ekwurlbe fails to teach or suggest that the sensitivity of cancer cells or a tumor to a chemotherapeutic agent can be increased by treatment with a compound as recited in the present claims. Moreover, Applicants

have shown unexpectedly superior results due to the synergistic interaction between dehydroequol and the chemotherapeutic agent.

Thus, Applicants respectfully request reconsideration and withdrawal of the rejections of Claims 1-4, 6-13, and 23-25 on the ground of nonstatutory obviousness-type double patenting over claims 1-21 of U.S. Patent No. 6,649,648 in view of Ekwurlbe.

2. Claims 1-4, 6-13, and 23-25 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-12 of copending Application No. 10/547,077 and claims 7-8 of copending Application No. 10/493390 in view of Ekwurlbe.

Application No. 10/493390 has been abandoned as of January 9, 2009. Thus, the Examiner is requested to withdraw the above double patenting rejection over claims 7-8 of Application No. 10/493390.

Regarding the rejection over claims 1-12 of copending Application No. 10/547,077 in view of Ekwurlbe, Applicants note that the rejection is merely provisional in nature, and defer responding until such time as allowable subject matter is identified. Furthermore, the October 2, 2003 international filing date of the present application is earlier than the November 19, 2004 filing date of copending Application No. 10/547,077. Accordingly, when the only rejection remaining in the present application is this obviousness-type double patenting rejection, the Examiner is requested to withdraw the rejection in accordance with MPEP 804(I)(*B*)(1).

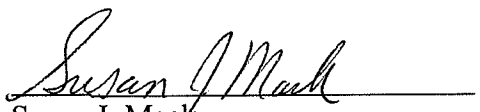
V. Conclusion

In view of the above, reconsideration and allowance of this application are now believed to be in order, and such actions are hereby solicited. If any points remain in issue which the

Examiner feels may be best resolved through a personal or telephone interview, the Examiner is kindly requested to contact the undersigned at the telephone number listed below.

The USPTO is directed and authorized to charge all required fees, except for the Issue Fee and the Publication Fee, to Deposit Account No. 19-4880. Please also credit any overpayments to said Deposit Account.

Respectfully submitted,



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